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A phase I dose-finding and pharmacokinetics study of CPC634 (nanoparticle entrapped docetaxel) in patients with advanced solid tumors.

Florence Atrafi, Herlinde Dumez, Ron H.J. Mathijssen, Catharina Wilhelmina Menke, Jo Costermans, Cristianne J.F. Rijcken, Rob Hanssen, Ferry Eskens, Patrick Schoffski; These authors contributed equally. Erasmus MC Cancer Institute, Rotterdam, Netherlands; Department of General Medical Oncology Leuven Cancer Institute, University Hospitals Leuven, KU Leuven, Leuven, Belgium; Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Medical Oncology, Cancer Center Amsterdam, Amsterdam, Netherlands; Cristal Therapeutics, Maastricht, Netherlands; Erasmus MC Cancer Institute, Rotterdam, Netherlands; Leuven Cancer Institute, University Hospitals Leuven, KU Leuven, Leuven, Belgium

Background: CPC634 is a novel product with docetaxel temporarily entrapped within stabilized CriPecR nanoparticles. We performed the first-in-human study with CPC634 (NCT02442531).

Methods: Patients (≥ 18 years) received CPC634 intravenously either 3-weekly (Q3W) (part 1, 15-100 mg/m²), 2-weekly (Q2W) (part 2, 45 mg/m²) or Q3W with dexamethasone premedication (part 3) following a 3+3 design. Primary objectives were to assess safety, establish the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and to evaluate the pharmacokinetic (PK) profile of CPC634. **Results:** Thirty-three patients (part 1; n = 24, part 2; n = 3, part 3; n = 6) were treated. Skin toxicity was dose limiting at doses > 60 mg/m² in part 1, and at a 45 mg/m² dose in part 2. Skin toxicity was cumulative but resolved after ceasing treatment. The MTD in part 1 was set at 70 mg/m². In part 3, the 60 mg/m² was explored which resulted in improved skin tolerability even after repeated administrations without dose limiting toxicities. The RP2D was therefore set at 60 mg/m² with dexamethasone premedication. Grade ≥ 3 adverse events (CTCAE version 4.03) were skin toxicity (21%), fatigue (8%), neutropenia (6%), peripheral sensory (8%) and motor neuropathy (4%), stomatitis (4%), infections (4%) and hypomagnesemia (3%). Alopecia grade 1 was reported in 15% of patients. CPC634 exhibited a dose-proportional PK profile. One partial response and sixteen cases of stable disease (RECIST 1.1) were confirmed in part 1 and in part 3 as best response. **Conclusions:** CPC634 could be administered safely but showed cumulative, though reversible skin toxicity at high doses. The RP2D was set at 60 mg/m² Q3W with dexamethasone premedication. Additional studies assessing the intratumoral exposure to CPC634 (NCT0371243) and a phase II efficacy study of CPC634 in patients with platinum resistant ovarian cancer (NCT03742713) is currently ongoing.